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FORMULATION AND EVALUATION OF CONTROL RELEASED BUCCAL PATCHES OF PROPRANOLOL

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Abstract:

Buccal drug delivery has been considered as an alternative to oral dosing for compounds subjected to degradation in the gastrointestinal tract or to hepatic first pass metabolism. Propranolol buccal patches were prepared by solvent casting technique using ethyl cellulose as baking membrane. . Propranolol buccal patches were prepared by using polymers like HPMC K15M,Guar gum, and karaya gum. Propylene glycol was used as plasticizer in the preparation of patches. Drug-excipients interaction studies (FTIR spectroscopy). The prepared patches will be evaluated for following parameter related to buccal drug delivery system like, a. Weight uniformity, b. Thickness. Folding endurance. Percentage swelling index,. Surface pH,of. Drug content estimation, g. Tensile strength,h. In-vitro drug release studies.In conclusion Propranolol buccal patches will be prepared to improve bioavailability and to avoid hepatic first pass metabolism. In all the cases the calculated standard deviation values are very low which they suggest that the prepared patches were uniform in weight. In all the cases the calculated standard deviation values are very low which suggest that, the prepared patches were uniform in thickness. From the result and conclusion of the research work we can summarize that propranolol can be delivered via buccal route.

Keywords: *Propranolol, HPMC, K15M, Gaur gum, karaya gum, propylene glycol and ethyl cellulose.*

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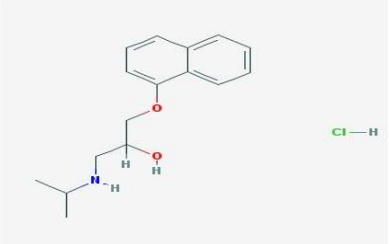
INTRODUCTION:

Oral administration of pharmaceutical compositions has some drawbacks. For instance, it is difficult to keep the medicament at the desired location so that it can be absorbed, distributed and metabolized easily. Accordingly, there has been much interest in the use of the mucosal lining of body cavities. Regions in the oral cavity where effective drug delivery can be achieved are buccal, sublingual, palatal and gingival. Buccal and sublingual sectors are the most commonly used routes for drug delivery and they may be used for the treatment of local or systemic diseases. . The permeability of the oral mucosa is probably related to the physical characteristics of the tissues . The buccal mucosa offers many advantages because of its smooth and relatively immobile surface and its suitability for the placement of controlled-release system which is well accepted by patients. The buccal mucosa is a useful route for the treatment of either local or systemic [1-5]

Need for the study

Advanced technique in biomaterials have resulted in the formulation of novel dosage form more pertinent to the oral cavity, meeting the challenges of the physiochemical properties of the drug entity itself and achieving the therapeutic aim of the drug delivery system. The buccal route has been used for many years to deliver drugs, which undergo first-pass metabolism. The buccal route has a relatively robust mucosa, has the advantage of allowing excellent accessibility, and reasonable patient compliance. Within the oral mucosal cavity, the buccal region offers attractive route of administration for local or systemic drug delivery. The mucosa has a rich blood supply and it is relatively permeable. Recently interest has been focused on the delivery of drug to or via mucous membrane by the use of mucoadhesive material, several mucoadhesive formulations are available under development and drug delivery via buccal mucosa is gaining importance of a novel route of drug administration. In the present study, various polymers such as HPMC K15M,Guar gum, and karaya gum were employed. These polymers are seen to be potential and comparatively economical.6-7



Structure of Propranolol

Description

Propranolol is a cationic amphiphilic molecule shown to block β_1 and β_2 adrenergic receptors with similar efficacy, without affecting α adrenergic receptors. Demonstrates high affinity for SR-1B (5-HT1B) receptors (K_i = 17nM), and milder affinity for SR-1D (5HT-1D) receptors (K_i = 10.2 μM). Propranolol hydrochloride also has been shown to inhibit the formation of phospholipase D-derived diacylglycerol (DAG) by inhibiting cytosolic phosphatides phosphohydrolase; making propranolol a useful tool for investigating phospholipase D-, and phospholipase C-mediated DAG production. Propranolol hydrochloride is an inhibitor of AR.

propranolol's IUPAC name i 1-naphthalen-1-yloxy-3-(propan-2-ylamino) propan-2-ols, with a molecular formula of $C_{16}H_{21}NO_2$ and a molecular weight of 295.80 g/mol. It is a Solid with Solubility in water (50 mg/ml), ethanol (10 mg/ml), DMSO (<14.5 mg/ml), and methanol. Pharmacodynamics of Propranolol, the prototype of the beta-adrenergic receptor antagonists, is a competitive, nonselective beta-blocker similar to nadolol without intrinsic sympathomimetic activity. Propranolol is a racemic compound; the l-isomer is responsible for adrenergic blocking activityDistribution volume of 4 L and More than 90% plasma protein binding rate. Propranolol is primarily metabolized by Hepatic system. Propranolol is extensively metabolized with most metabolites appearing in the urine. With half-life of approximately **4** hours.[8-10]

MATERIALS AND METHODS:

The preparation of fluconazole buccal tablets involves a variety of ingredients sourced from reputable suppliers. The active pharmaceutical ingredient Propranolol is supplied by Gift Sample from Cipla Pvt. Ltd., Mumbai . Excipients such as, HPMC K100M , Guar gum, are procured Loba Chemical Pvt. Ltd., Mumbai. Karaya gum, Propylene glycol supplied by Astra Zeneca Pvt. Ltd., Bangalore. Ethanol, Pot. Dihydrogen O-phosphate, Mercury are supplied by SD Fine Chem., Mumbai. And Sodium hydroxide excipient is supplied by Changshu Yangyuan chemicals, China.

The manufacturing process utilizes several key pieces of equipment. An Digital balance BT 220H, Shimadzu Corporation ensues accurate measurement of ingredients. A Friabilator EF-2 from Electrolab, Mumbai, tests tablet friability. The Electro lab, disintegration of apparatus of ED-2L, Inco Instruments, Mumbai used to evaluates the disintegration profile of the patches. The PH meter supplied by Systronics pH system 361. The sanicator supplied by Remi Equipments, Mumbai.The Thickness tester supplied by Screw Gauze .The UV

Visible spectrophotometer of 1700, Shimadzu Corporation, Japan used and for tensile strength , Tensile Strength tester of (model no :Tinius Olsen (HT400) . Finally, FTIR (model no and source :Jasco FTIR410). [11-13]

Methodology

Preparation of backing layer

For preparing a formulation, a glass petri plate of 7.5 cm diameter was used as a casting surface. Initially, backing membrane of ethyl cellulose was fabricated by slowly pouring a solution containing 750 mg of ethyl cellulose and 4 drops Propylene glycol in 10 ml Dichloromethane and Methanol (1:1) to the glass petri plate. Mercury was used as a substrate and air dried for 9 hrs.[14]

Preparation of Propranolol buccal patches (Incorporation of drug):

The calculated amount of Propranolol was incorporated in the polymeric solutions of different concentrations of (xanthan gum, guar gum, karaya gum) by using DCM:Methanol in 1:1 ratio and after levigation with 30 % propylene glycol and then the permeation enhancer and sweetening agent were added. The solution was casted onto preformed ethyl cellulose baking layer then kept in hot air oven at 40°C for 24 hrs (or at room temperature). The patches thus formed were cut into size of 10 mm diameter. Each patch contains 10 mg of Propranolol. The detailed compositions of the Propranolol patches are given in below Table

Formulation of backing layer

Ethyl cellulose(mg)	750	1000
Propylene glycol	4 drops	4 drops
Dichloromethane: Methanol(ml) 1:1	10	10

Formulation Composition

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propronolol	100	100	100	100	100	100	100	100	100
Guar gum(mg)	150	250	300						
HPMC k100M(mg)				150	250	300	-	-	-
Karaya Gum (mg)	-	-	-	-	-		150	250	300
Propylene glycol	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml
Aspartame (Mg)	2	2	2	2	2	2	2	2	2
Citric acid	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
DCM : Methanol (ml)	15	15	15	15	15	15	15	15	15

Evaluation of Buccal Patches

Physical properties [16-18]

a) Physical appearance and surface texture of patch

This parameter was checked simply with visual inspection of patches and evaluation of texture by feel or touch

.b) Weight uniformity of patches

Three patches of the size 10 mm diameter were weighed individually using digital balance and the average weights were calculated.[15]

c) Thickness of patches

Thickness of the patches was measured using screw gauge with a least count of 0.01 mm at different spots of the patches. The thickness was measured at three different spots of the patches and average was taken.

d) Folding endurance of patches

The flexibility of patches can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the patches was determined by repeatedly folding (10 mm) patches at the same place till it broke. The number of times patches could be folded at the same place, without breaking gives the value of folding endurance.

e) Swelling index of patches:

The swelling index of the patches was determined by immersing Preweighed patch of size 10 mm in 50 ml water. The patches were taken out carefully at 5, 10 upto 30 min. intervals, blotted with filter paper and weighed accurately.

The swelling index calculated by,

$$\text{Swelling Index} = \frac{\text{Weight of the swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}}$$

f) Surface pH of patches:

Surface pH was determined by the patches were allowed in contact with

1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing equilibrate for 1 min.

2. Mechanical properties

a) Tensile strength of patches:

Tensile strength of the patch was determined with digital tensile strength tester (Tinius-Olsen). The sensitivity range of the machine is 1-10 Newton's. It consists of two load cell grips. The lower one was fixed and upper one was movable. The test patch of size (1x4 cm2) was fixed between these cell grips and force was applied till it breaks. The tensile strength of the patch was directly taken from the dial reading in Newton's, which was converted into kilogram.

Tensile Strength Tester

Evaluation of Propanolol buccal patches

a) Drug content uniformity study of patches [17]

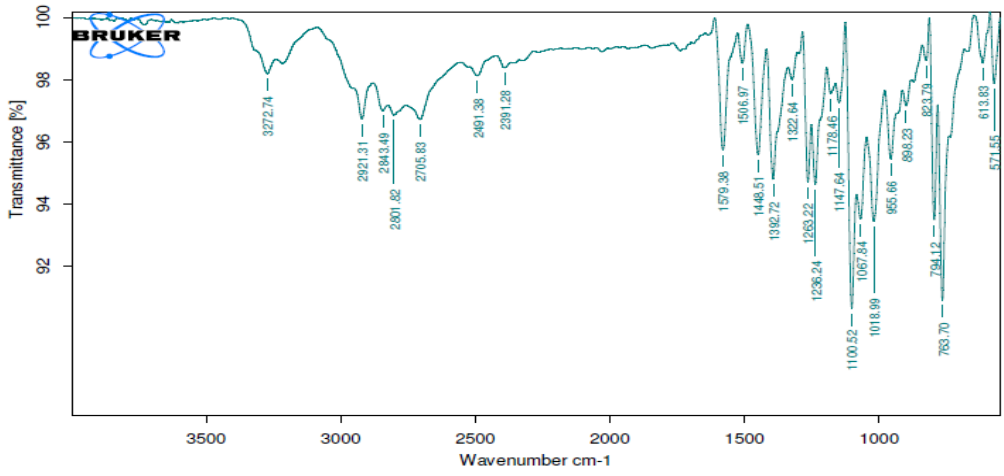
The patches were tested for drug content uniformity by UV Spectrophotometric method. Patches of 10 mm diameter were cut from three different places from the casted patches. Each patch was placed in 100 ml volumetric flask and dissolved in pH 6.8 phosphate buffer and 0.2 ml is taken and diluted with pH 6.8 phosphate buffer upto 10 ml. The absorbance of the solution was measured at 318 nm using UV/visible spectrophotometer (Shimadzu UV-1700). The percentage drug content was determined using the standard graph and the same procedure was repeated for three patches.

b) *In-vitro* drug release of patches

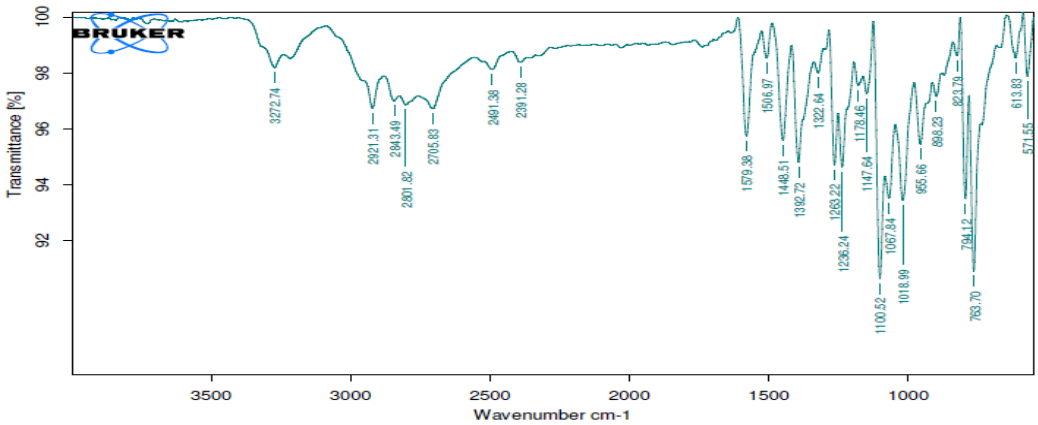
In-vitro release studies were carried out by attaching sigma dialysis membrane to one end of the open cylinder which acted as donor compartment prepared buccal patches containing drug was placed inside donor compartment which is agitated continuously using magnetic stirrer and then temperature was maintained at 37 ± 1ºC. Receptor compartment consist of 100 ml of pH 6.8 phosphate buffer, sample of 2 ml were withdrawn at periodic intervals from receptor compartment and replaced with fresh pH 6.8 phosphate buffer immediately, and drug release was analyzed spectrophotometrically at 318 nm. Release rate was studied for all prepared formulations.[18]

RESULTS AND DISCUSSION:

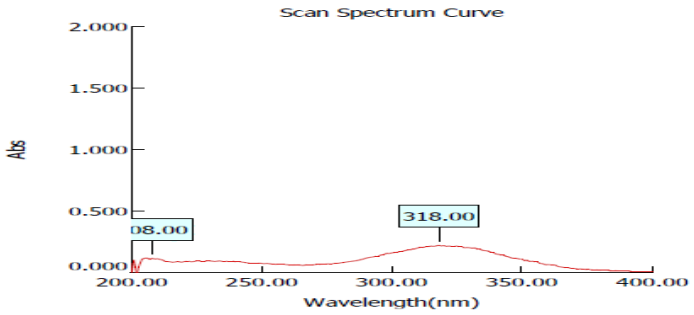
Drug-excipients interaction studies of patches



FTIR Spectra of Propranolol (pure drug)



FTIR Spectra of optimized formulation



UV Spectrum of Propranolol

Calibration Curve Of Propranolol in 6.8 pH Buffer

S. NO.	Concentration(µg/ml)	Absorbance
1	0	0
2	2	0.182
3	4	0.321
4	6	0.466
5	8	0.625
6	10	0.768
7	12	0.942

The weight of the patches was determined using digital balance and the average weight of all patches was given in Following Table [19]

Formulation code	Drug content	Thickness	Folding endurance	Surface pH	Wt.variation	Disintegration time(S)
F1	85.20	0.38	294	6.2	48.21	88
F2	88.42	0.41	286	6.8	50.26	96
F3	90.16	0.46	240	6.8	49.84	102
F4	72.18	0.52	190	6.6	56.4	81
F5	81.64	0.48	220	6.8	52.06	86
F6	85.52	0.52	225	6.6	50.24	89
F7	87.98	0.48	268	6.5	41.2	51
F8	92.46	0.52	280	6.8	44.6	57
F9	95.42	0.46	295	6.8	51.3	71

Swelling Index (%) of mucoadhesive buccal patches of Propranolol.

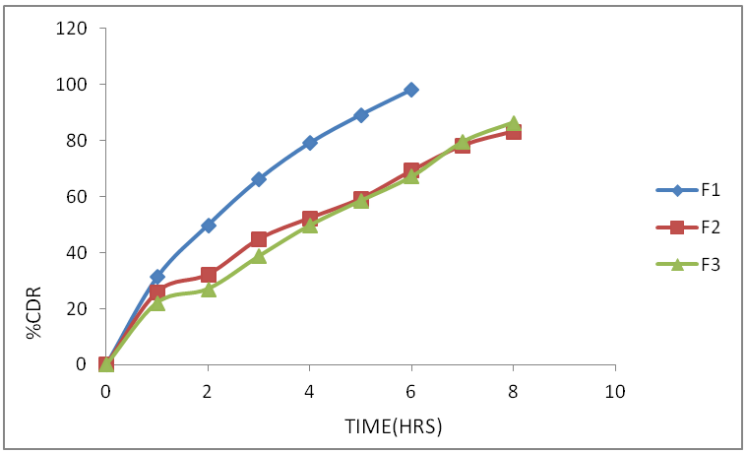
FC	Avg. Swelling Index (%) ± SD, n=3
F1	40.15 ± 1.537
F2	32.65 ± 1.358
F3	38.01 ± 1.746
F4	29.93 ± 1.100
F5	41.16 ± 1.242
F6	37.64 ± 0.996
F7	48.16 ± 1.02
F8	36.64 ± 0.91
F9	42.16 ± 1.46

Tensile strength of mucoadhesive buccal patches of Propranolol

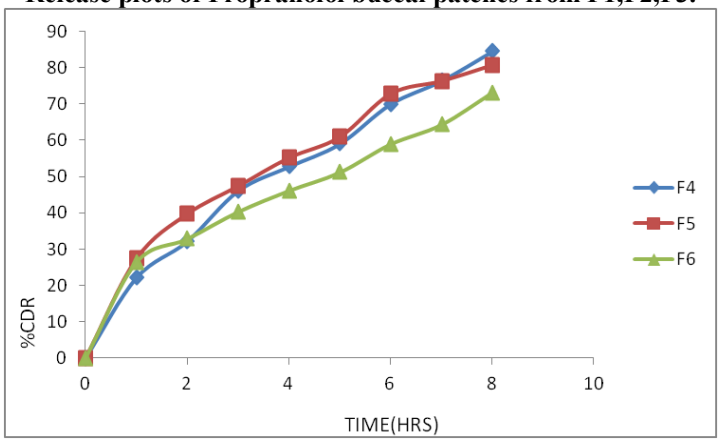
FC	Avg. Tensile Strength (kg/cm) ± SD, n=3
F1	4.833 ± 0.305
F2	5.566 ± 0.208
F3	6.233 ± 0.251
F4	4.568 ± 0.152
F5	5.236 ± 0.251
F6	6.366 ± 0.115
F7	4.528 ± 0.16
F8	5.281 ± 0.25
F9	6.352 ± 0.12

Drug release data at the end of 8 hrs from Propranolol buccal patches

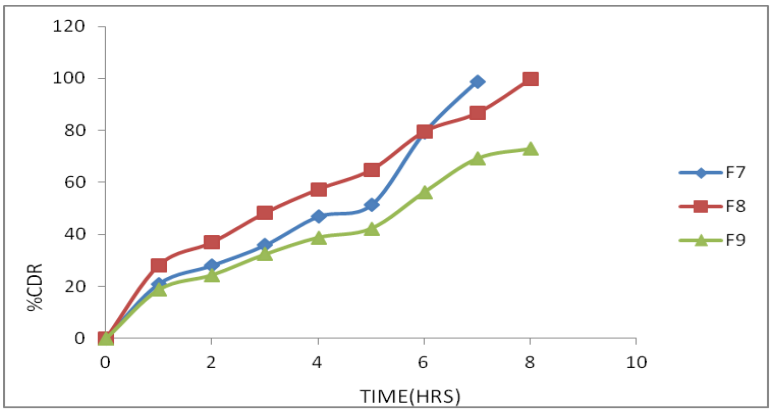
TIME	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	31.28	25.96	22.12	22.12	27.36	26.39	21.02	28.21	18.82
2	49.89	32.22	27.06	32.16	39.67	32.81	28.02	36.94	24.42
3	66.29	44.82	38.75	46.04	47.33	40.24	35.81	48.29	32.38
4	79.23	52.32	49.74	52.73	55.11	46.06	46.8	57.32	38.81
5	89.28	59.28	58.51	59.02	60.86	51.12	51.26	64.82	42.28
6	98.24	69.26	67.16	69.97	72.74	58.89	79.16	79.52	56.26
7		78.21	79.55	76.37	76.24	64.25	98.91	86.66	69.16
8		83.26	86.45	84.47	80.62	73.11		99.64	72.91



Release plots of Propranolol buccal patches from F1,F2,F3.



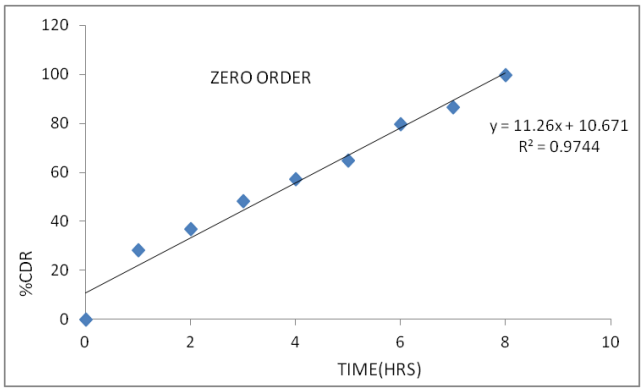
Release plots of Propranolol buccal patches from F4,F5,F6.



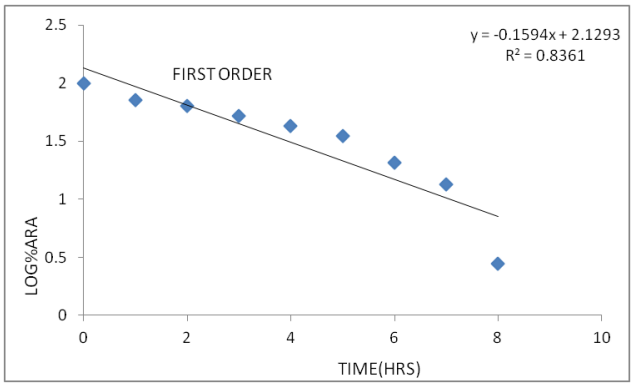
***In-vitro* Drug release of Buccal Films of Formulations F7-F9**

Kinetic data of Propranolol mucoadhesive buccal patches

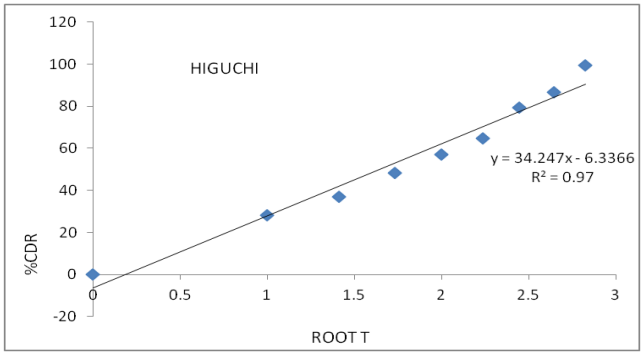
Zero order



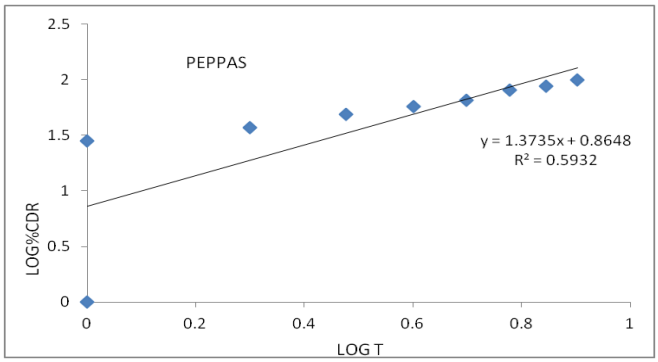
First Order



Higuchi plot



Peppas Plot



R^2 values					n values
Formulation	**Zero order**	**First order**	**Higuchi**	**Korsmeyer - Peppas**	**Korsmeyer-Peppas (n)**
F8	**0.974**	**0.836**	**0.97**	**0.593**	**1.37**

The invitro dissolution data for best formulation F8 were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer-peppas equation. Optimized formulation F8 shows R^2 value 0.974. As its value nearer to the '1' it is conformed as it follows the Zero order [20] release. The mechanism of drug release is further confirmed by the Higuchi and peppas plot, if n = 0.45 it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavior or non-Fickian transport, n = 0.89 for case II transport and n > 0.89 for Super case II transport.

The 'n' value is 0.826 for the optimised formulation(F8) i.e., n value was > 0.89 this indicates Super case II transport. The release kinetics for the optimized formula are shown in table.

SUMMARY AND CONCLUSION:

The results are quoted in different section of chapter-03 from the result of various evaluation parameters, we can summarize:

1.The patches prepared were checked visually for its appearance and surface

2.texture. All the prepared patches were of smooth surface and elegant texture.

3.All the prepared patches using different concentration of various polymers are weighing in between 150 to 300 mg.

4. The patches show thickness values in between 0.38 to 0.52 mm.

5. The patches show folding endurance values in between 190 to 258 The patches show swelling index values in between 29.93 to 48.16 %

.7. Similarly surface pH of all the patches prepared is ranging in between6.2 to 6.8 pH.

8. The tensile strength of all the patches prepared is ranging in between 4.52 to 6.35 Kg/cm2 respectively.

9. The FTIR studies indicate that propranolol showed complete entrapment within the polymer carrier bonding is suggested and there were no chemical interaction.

10.Similarly, the patches are also subjected to drug content uniformity study and it lies in between 855.20to 95.42 %, which suggest that uniform dispersion throughout the buccal patches.

11.Finally the *in-vitro* drug release study was carried out for all the patches and release profile were subjected to various kinetic equations like Higuchi diffusion equation and Peppas exponential equation. The regression coefficient values of this kinetic equation are very nearer to one (1) suggesting that plots are fairly linear and slope values of the Peppas equation is (>1) suggest that drug was released by diffusion mechanism following super caseII transport.

From the above results it can be concluded that propranolol can be delivered in the form of buccal patches. Release pattern of drug from these patches can be altered by using different formulation variables.

From the present research work that is development and evaluation of propranolol patches for buccal drug delivery, the following points can be concluded:

The patches prepared were elegant in appearance and smooth surface.

The weights of patches and the thicknesses were uniform. The patches were completely dried. The patches had good flexibility. The patches shows uniform swelling index.

The surface pH of the patches was uniform. The patches show uniform tensile strength.

There was no drug-excipients interaction between the drug and excipients used in the formulation.

The drug was distributed throughout the patch uniformly.

More than 99 % of the drug was released from all the formulation f8 at the end of 8th hrs.

From the result and conclusion of the research work we can summarize that propranolol can be delivered via buccal route.

REFERENCES:

1. Jain N.K. Controlled and Novel Drug Delivery, 1st edition, published by CBS Publishers and Distributors, New Delhi. 1997; 52-81.

2.Shojaei AH. A systemic drug delivery via the buccal mucosal route, Pharm. Tech. 2001; 70-81.

3.Kharenko EA, Larionva NA, Demina NB. Mucoadhesive drug delivery system: quantitative assessment of interaction between synthetic and

natural polymer films and mucosa. 2008; 42 (7): 17-24.
4.Patel VM, Prajapati BG, Patel MM. Design and characterization of chitosan containing mucoadhesive buccal patches of propranolol hydrochloride. Acta pharm. 2007; 57: 61-72.
5.Noha AN, Fatma AI, Boraie NA, Mortada LM. Mucoadhesive buccal patches of miconazole nitrate: *in-vitro/ in-vivo* performance and effect of aging. Int. J. pharm. 2003; 264: 1-14.
6.Amir H. Shojaei. Buccal mucosa as a route for systemic drug delivery: A review; J. Pharm. Sci.1998; 1 (1): 15-30.
7.Tora-Tora Derrikson principles of anatomy and physiology 2nd edition, edited by Bonnie Roech, Published by John wily and sons Inc. 2007; 902-08
8.Ross and Wilson. Anatomy and physiology in health and illness 9th edition edited by Anne Waugh and Alison Graw Published by Churchill Livingstone, Edinberg. 2001; 289-93.
9. Chatterjee CC. Human anatomy and physiology 10th edition Publishedby medical alliend agency, Calcutta 1985; 427-35.
10.Kharenko EA, Larionova NI, Demina NB. Mucoadhesive drug delivery system (review). Pharm. Chem. J. 2009; 43 (4): 200-09.
11. http://mota.stanford.edu/education/physics%2087N%20final%20Projects /Group%20Beta/drug03.htm.
12. Pharmaceutics the science of dosage form Design 2nd edition edited by M. E. Aulton. Published by Harcourt publishers Limited. 2002; 198-200.
13.Bristol-Myers Squibb Company, Syracuse. Oral cavity as a site for bioadhesivedrug delivery. Advanced drug delivery reviews, 1994; 13: 43-74.
14.Dominique Duchene and Gilles Ponchel. Bioadhesion of solid oral dosage form, why and how. Euro. J. Pharm. Biopharm. 1997; 44: 15-23.
15. Applied Biopharm. and pharmacokinetics 5th edition, edited by Leon Shargel . Published by M.C Grave hill companies 2005; 371-74.
16.Artusi M, Santi P Colombo P, Junginger HE. Buccal delivery of thiocolchicoside: *in-vitro* and *in-vivo* permeation studies. Int. J. Pharm. 2003; 250: 203-13.
17. Novel Drug Delivery system. 2nd edition, edited by James Swarbrick, Published by Marcel nokker Inc. 2007; 197-24.
18. Advances in controlled and Novel drug delivery and physiology 4th edition edited by Bonnie Roesch. Published by John wily and sons Inc.2007; 70-82.
19. Luana P, Valeria A, Fausta A, Maurizio R, Stefano G, Marinella C, Carlo R. Development of mucoadhesive patches for buccal administration of ibuprofen. J. Cont Rel. 2004; 99: 73-82.
20. Isabel Diaz, Francoise F, Richard HG, Yves J. *Ex-vivo* evaluation of bioadhesive films for buccal delivery of fenatyl. J. Cont Rel. 2007; 1-15.